Nasal mucosal melanosis may act as a harbinger of melanoma: A case report

Nasal mucosal melanosis may act as a harbinger of melanoma: A case report

William C. Yao, M.D.,[1,2] Kevin S. Emerick, M.D.,[2] Stefan Kraft, M.D.,[3] and Eric H. Holbrook, M.D.[2]

ABSTRACT

Background: *The progression from a benign pigmented lesion on the skin to cutaneous melanoma is better understood, and it could be presumed that a similar progression occurs with mucosal lesions. However, to our knowledge, there has never been documentation of melanosis transforming into melanoma over time.*

Objective: *To describe a transformation of a mucosal melanosis into melanoma.*

Methods: *A 53-year-old man with diffuse melanosis of the nasal cavity underwent surgical resection.*

Results: *Pathology revealed melanocytic hyperplasia without evidence of melanoma. The patient was serially examined, with excisions for new areas of melanosis. The pathology progressed to severely atypical melanocytic proliferation and melanoma* in situ *over a 4-year period.*

Conclusion: *Nasal melanosis may be a precancerous lesion and may transform into melanoma. All melanosis should be biopsied with close endoscopic observation. Lesions with dysplasia or atypia should be excised due to potential transformation to melanoma.*

(Allergy Rhinol 7:e164–e167, 2016; doi: 10.2500/ar.2016.7.0174)

Sinonasal melanosis is a mucosal pigment deposition that is often associated with a proliferation of melanocytes in a single area. Unlike individuals of African decent with dark skin, pigmentation is rarely encountered in the nasal mucosa except in the olfactory area in the white population. In 1974, Zak and Lawson[1] identified melanocytes in the nasal mucosa, mucous glands, and superficial and deep stroma of the nasal cavity. Although the origin of the melanocytes is unclear in the nasal cavity, their presence explained the occurrence of primary nasal mucosal melanomas. To date, there are literature and experience that show melanosis in a melanoma specimen.[2] Moreover, melanosis without an invasive component is frequently encountered in patients with metastatic malignant melanoma. However, to our knowledge, there has never been documentation of melanosis transforming into melanoma over time. The patient was seen at the Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts (institutional review board exempt: 15–004H).

From the [1]Department of Otorhinolaryngology, University of Texas McGovern Medical School—Houston, Houston, Texas, [2]Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts, and [3]Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

No external funding sources reported

The authors have no conflicts of interest to declare pertaining to this article

Address correspondence to William C. Yao, M.D., University of Texas Medical School at Houston, 6431 Fannin Street, MSB 5.036, Houston, TX 77030

E-mail address: william.c.yao@uth.tmc.edu

CASE PRESENTATION

B.S. was a 53-year-old white man who presented for diffuse nasal melanosis of the left nasal cavity and inverted papilloma of the left middle turbinate. The patient had a nasal biopsy performed by the referring otolaryngologist, which revealed melanocytes without malignant features in addition to a separate inverting papilloma of the left middle turbinate. After discussion at a multidisciplinary melanoma tumor board, the decision was made for complete excision of the involved nasal mucosa. The patient underwent extensive resection of the nasal melanosis to the level of the underlying bone, with 5-mm margins, as well as the removal of his left middle turbinate as part of the inverting papilloma excision. Pathology revealed extensive melanosis, with foci of melanocytic proliferation and a small area in the left middle turbinate with focal severely atypical melanocytic proliferation. The margins were free of melanosis. After the surgery, the patient was closely monitored with serial nasal endoscopy. Melanosis recurred in 18 months, for which he underwent a second excision. Pathology revealed melanosis abutting the margins but without any evidence of malignancy.

Melanosis recurred a few months later with the previously resected border extending onto the frontal recess. The patient underwent a modified Lothrop procedure and further removal of melanotic foci. Pathology revealed melanocytic hyperplasia. His melanosis recurred in 6 months, at which time the excised pathology revealed focal moderately to severely atypical intraepithelial melanocytic proliferation. The case was re-presented at the melanoma

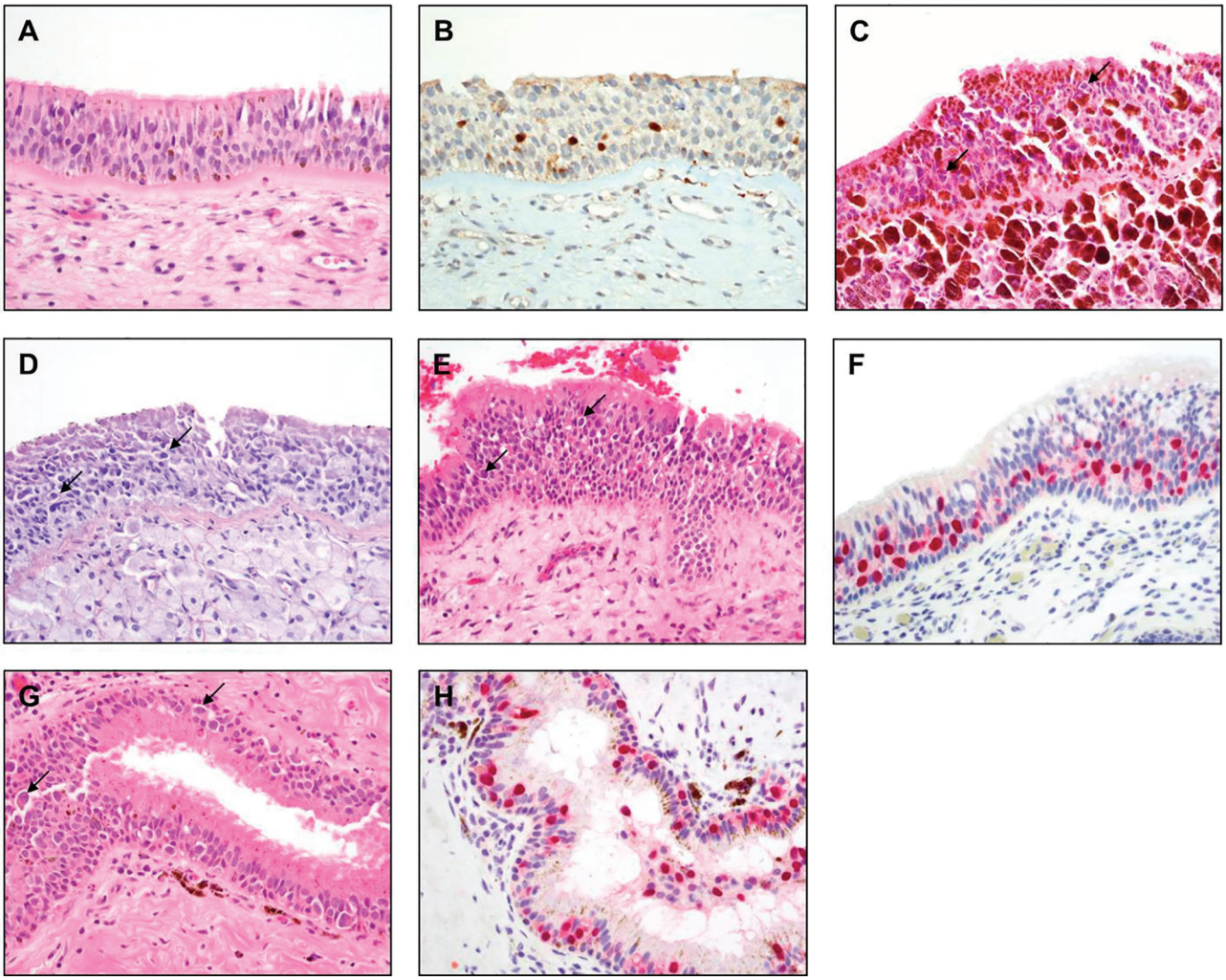

Figure 1. (A) Melanosis with melanocytic hyperplasia (hematoxylin and eosin [H&E], original magnification ×400). Sinonasal mucosa with melanin deposition in respiratory epithelial cells and in subepithelial macrophages. Intraepithelial melanocytes are not clearly distinguishable from epithelial cells and lack cytologic atypia. (B) Melanosis with melanocytic hyperplasia (microphthalmia transcription factor [MITF] stain, original magnification ×400; peroxidase). Scattered melanocytes are seen, which exhibit nuclear staining; the nuclei are not enlarged. (C) Melanosis with atypical intraepithelial melanocytic proliferation (H&E, original magnification ×400); there is intense melanin pigment deposition in epithelial cells; numerous melanin-containing macrophages are present in subepithelial tissue; occasional melanocytes can be seen (arrows); they show enlarged atypical nuclei with prominent nucleoli. (D) Melanosis with atypical intraepithelial melanocytic proliferation (melanin bleach, original magnification ×400); numerous subepithelial foamy histiocytes are seen; occasional atypical intraepithelial melanocytes are present (arrows). (E) Melanoma in situ (H&E, original magnification ×400); the melanocytic proliferation shows an (E) Melanoma in situ (H&E, original magnification ×400); the melanocytic proliferation shows an increased density; melanocytes (arrows) are enlarged and exhibit atypical enlarged nuclei with prominent nucleoli. (F) Melanoma in situ (MITF, original magnification ×400; alkaline phosphatase); the MITF shows a dense intraepithelial melanocytic proliferation; melanocyte nuclei are enlarged. (G) Melanoma in situ within glands (H&E, original magnification ×400); there is a confluent melanocytic proliferation; melanocytes (arrows) are enlarged, pleomorphic, and exhibit atypical enlarged nuclei with prominent nucleoli. (H) Melanoma in situ within glands (MITF, original magnification ×400; alkaline phosphatase); the MITF stain shows dense growth of intraepithelial melanocytes with enlarged nuclei.

tumor board, and the consensus decision was to resect new foci of melanosis as it appears. Five years after the original removal of the melanotic tissue, B.S. underwent excision for recurrent melanosis. Pathology revealed severely atypical melanocytic proliferation in the frontal recess and nasal septum; however, there was melanoma *in situ* arising in the background of nasal melanosis at the left anterior maxillary sinus. The tumor board consensus was for continued observation with excision of any new melanotic lesions. B.S. had since developed new areas of melanosis without dysplasia in his nasal cavity, which required surgical excisions. He continued to live without any further progression into invasive

malignant melanoma. He also did not have any evidence of regional or distant metastases.

DISCUSSION

Sinonasal mucosal melanoma is a rare but aggressive form of malignancy associated with a poor prognosis. No precursor lesions for mucosal melanosis are known, although associations with melanosis have been made. Mucosal melanoma is believed to arise from the metaplasia of a preexisting melanocyte in the nasal cavity.[1] To date, a sequential progression of nasal mucosal melanosis into melanoma *in situ* has not been described. For *de novo* genesis of sinonasal melanoma, melanocytes need to be present within the nasal mucosa. Nasal mucosal melanosis is most commonly observed in the olfactory area but rarely in other areas of the nasal cavity. However, the majority of sinonasal melanoma occurs in the septum, inferior turbinate, and lateral nasal wall.[3]

One previously accepted theory for mucosal melanoma formation was that the mucosal lining underwent squamous metaplasia that led to the pluripotent squamous cells forming melanocytes. Several cases showed nasal melanomas occurring in stratified squamous lining instead of the pseudostratified columnar cells.[4] However, Allen and Spitz[5] identified junctional changes consistent with melanocytic hyperplasia within the pseudostratified columnar cell lining, which showed that squamous metaplasia does not have to occur for melanocyte formation. Moreover, in a histologic analysis, melanocytes were identified within the deep stroma of the nasal mucosa. For melanotic pigment to appear to the naked eye, the previously dormant stromal melanocyte needs to migrate peripherally.[1] The peripheral migration of melanocytes can be considered an abnormal process, which can explain the low incidence of mucosal melanosis in patients without mucosal melanoma. Lewis and Martin[6] examined the pigmentation of the nasal mucosa in Ugandan Africans. Ectopic pigment was found in 13.5% of the individuals examined, with the most common area being the nasal septum. The incidence of melanoma in the melanotic lesions biopsied was 2.6%. A correlation existed between the area of benign pigmentation and the site of nasal mucosal melanoma, which raised the possibility that melanoma may arise *via* malignant transformation of pigmented areas with high melanocyte concentration.

Our patient initially presented with melanosis and underwent a wide local excision of all clinically affected areas. Initially, the lesion only contained areas of melanocytic proliferation with dysplasia. In all the cases, the surgical specimens were reviewed by a pathologist (S.K.) who specializes in examining pigmented tumors. Although the criteria for sinonasal melanoma *in situ* are not well defined, the specimens with "focal severely atypical melanocytic proliferations" had severe cytologic atypia but lacked the density and confluent growth required for mucosal melanoma *in situ*, which leads to a thought that melanocyte proliferation can undergo dysplastic changes. One study examined the pathologic specimen of 32 patients with previously diagnosed sinonasal mucosal melanoma.[7] The investigators identified melanoma *in situ* in 67% of the specimens and melanocytic hyperplasia in 16% of the specimens. More than 80% of the melanoma specimens contained nests of intraepithelial melanocytic proliferations. Because intraepithelial melanocytic proliferations are commonly present in melanoma specimens, there is a possibility that these lesions may indeed be premalignant lesions that can eventually progress into malignant sinonasal melanoma.

Contrary to sinonasal melanosis, conjunctival primary acquired melanosis occurs more frequently and has been studied more extensively.[8–10] These lesions are commonly biopsied and treated with observation or surgical resection. Shields *et al.*[10] performed a review of 311 patients with conjunctival primary acquired melanosis. They found 35% of the lesions to enlarge in size and 12% transformed into melanoma when clinically observed over a 10-year period.[10] For lesions that were initially biopsied, the mean interval to developing melanoma was 39 months and a 13% risk of progressing to a melanoma when there was evidence of severe atypia. Another study noted a 32% overall risk of malignant transformation into melanoma that increased to 46% with the presence of any atypia.[8] Both studies identified lesions that progressed to melanoma when there was evidence of atypia in the original biopsy. The study by Shields *et al.*[10] recommended complete surgical excision if the lesion was occupying more than 2 hours in size with meticulous follow-up.

The findings from the ophthalmologic literature likely have some translatable experience that can be applied to sinonasal melanosis. All melanotic lesions should undergo at least a biopsy with serial examination. An excision should be performed when there is the presence of atypia due to the increased risk of malignant transformation. In our patient, the melanosis exhibited evidence of dysplasia in the initial excision. Over time, the patient developed multiple recurrences of melanosis that eventually progressed into melanoma *in situ* (Fig. 1). The presence of recurrent melanosis may signify an underlying abnormality in the nasal mucosal cell signaling that caused areas of melanocytic overproliferation. With increased melanocytic proliferation, increased mutation errors can occur, thereby increasing the risk of malignant transformation. Therefore, nasal melanosis should be treated as a precancerous lesion.

We propose a treatment algorithm for intranasal melanosis based on the finding in our patient. All intranasal melanosis should at least undergo a biopsy. If there are multiple areas of melanosis or evidence of atypia on biopsy, an excision with negative margins should be performed. Moreover, the patient needs to be closely monitored due to the frequent recurrence of melanotic lesions. Recurrent lesions should be biopsied or excised.

CONCLUSION

Nasal melanosis may act as a precancerous lesion and transform into melanoma. Until now, melanosis that transforms into melanoma has, to our knowledge, never been described or documented. All nasal melanosis should be biopsied or excised with close endoscopic observation. When there is evidence of dysplasia or atypia, lesions should be aggressively treated with wide local excision due to potential transformation to melanoma.

REFERENCES

1. Zak FG, and Lawson W. The presence of melanocytes in the nasal cavity. Ann Otol Rhinol Laryngol 83:515–519, 1974.
2. Hofbauer GF, Boni R, Simmen D, et al. Histological, immunological and molecular features of a nasal mucosa primary melanoma associated with nasal melanosis. Melanoma Res 12:77–82, 2002.
3. Clifton N, Harrison L, Bradley PJ, and Jones NS. Malignant melanoma of nasal cavity and paranasal sinuses: Report of 24 patients and literature review. J Laryngol Otol 125:479–485, 2011.
4. Ravid JM, and Esteves JA. Malignant melanoma of the nose and paranasal sinuses and juvenile melanoma of the nose. Arch Otolaryngol 72:431–444, 1960.
5. Allen AC, and Spitz S. Malignant melanoma; a clinicopathological analysis of the criteria for diagnosis and prognosis. Cancer 6:1–45, 1953.
6. Lewis MG, and Martin JA. Malignant melanoma of the nasal cavity in Ugandan Africans. Relationship of ectopic pigmentation. Cancer 20:1699–1705, 1967.
7. Mochel MC, Duncan LM, Piris A, and Kraft S. Primary mucosal melanoma of the sinonasal tract: A clinicopathologic and immunohistochemical study of thirty-two cases. Head Neck Pathol 9:236–243, 2015.
8. Folberg R, and McLean IW. Primary acquired melanosis and melanoma of the conjunctiva: Terminology, classification, and biologic behavior. Hum Pathol 17:652–654, 1986.
9. Shields CL, and Shields JA. Conjunctival primary acquired melanosis and melanoma: Tales, fairy tales, and facts. Ophthal Plast Reconstr Surg 25:167–172, 2009.
10. Shields JA, Shields CL, Mashayekhi A, et al. Primary acquired melanosis of the conjunctiva: Experience with 311 eyes. Trans Am Ophthalmol Soc 105:61–71; discussion 71–72, 2007. □